CHEMOTHERAPY – RELATED TUMOUR LYSIS SYNDROME

BY DR. N. W. BUSAKHALA
Definition
Two types of tumour lysis syndrome (TLS);

1. **Laboratory TLS:**
   - 25% increase in potassium, phosphate and uric acid, or decline in calcium from baseline.
   - Occur within 4 days of initiating chemotherapy.
   - Patients on standard of care.
   - Minimum of two out of four criteria.

Hande and Garrow 1993
2. Clinical tumour lysis syndrome

Laboratory TLS plus renal failure, cardiac arrhythmias or sudden death.

- A new definition has been suggested by Cairo and Bishop to include values above upper limit of normal.

- Study used Hande and Garrow definition.

Cairo and Bishop 2004
PREDICTORS OF TLS

- Tumor factors
- Treatment factors
- Patient factors

<table>
<thead>
<tr>
<th>STUDIES ON TLS</th>
<th>Incidence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hyperuricemia</strong></td>
<td>14%-70%.</td>
<td>Haas 1999 emedicine.com 2003</td>
</tr>
<tr>
<td><strong>Azotemia</strong></td>
<td>3- 7.5%</td>
<td>Carl et al, Arch Inter Med. 1974;133:349-359</td>
</tr>
</tbody>
</table>
METHODOLOGY

- Serum potassium, phosphate, uric acid and calcium were determined on day 1 and then 24 hourly for 4 days.

- Tests were repeated on the 7th day in those developing TLS to check resolution.

- If no resolution, tests were repeated on the 15th day.
METHODOLOGY CTD

Inclusion Criteria
• Patients aged 13 years and above
• Tissue diagnosis of cancer.
• Patients receiving the first course of chemotherapy.

Exclusion Criteria
• Patients on treatment for gout.
• Post-renal transplant patients.
• Unwillingness to come back to the Hospital for four consecutive days.
• Dehydrated patients.
366 files of cancer patients

208 chemotherapy prescribed

187 Qualified

142 Recruited

111 Completed study

25 No chemo received

69 TLS -ve

42 TLS +ve

21 GFR < 90ml/min

45 Excluded

158 Radiotherapy

6 Incomplete follow up
RESULTS
<table>
<thead>
<tr>
<th>TUMOUR</th>
<th>Number</th>
<th>STAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>8</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>II</td>
</tr>
<tr>
<td>Hodgkin’s lymphoma</td>
<td>2</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>III</td>
</tr>
<tr>
<td>Chronic lymphocytic Leukemia</td>
<td>8</td>
<td>IV</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>18</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>I</td>
</tr>
<tr>
<td>Others</td>
<td>13</td>
<td>IV</td>
</tr>
<tr>
<td>No staging (AML, ALL, MM)</td>
<td>21</td>
<td>-------</td>
</tr>
<tr>
<td>Total</td>
<td>111</td>
<td>-------</td>
</tr>
</tbody>
</table>
### Serum Electrolyte Changes

<table>
<thead>
<tr>
<th></th>
<th>DAY 1</th>
<th>DAY 2</th>
<th>DAY 3</th>
<th>DAY 4</th>
<th>DAY 7</th>
<th>DAY 15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Potassium</strong></td>
<td>24.7</td>
<td>30.1</td>
<td>32.5</td>
<td>28.8</td>
<td>28.6</td>
<td>14.7</td>
</tr>
<tr>
<td><strong>Phosphate</strong></td>
<td>73.5</td>
<td>88.3</td>
<td>95.7</td>
<td>94.2</td>
<td>56.8</td>
<td>13.3</td>
</tr>
<tr>
<td><strong>Calcium</strong></td>
<td>-2.2</td>
<td>0.9</td>
<td>1.2</td>
<td>0.7</td>
<td>1.8</td>
<td>5.3</td>
</tr>
<tr>
<td><strong>Uric Acid</strong></td>
<td>4.1</td>
<td>5.5</td>
<td>4.1</td>
<td>3.9</td>
<td>2.6</td>
<td>-4.0</td>
</tr>
</tbody>
</table>

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**SERUM ELECTROLYTE CHANGES**

The graph illustrates the percentage median change in various serum electrolytes over different days of observation. The table below corresponds to the graph, showing the changes in potassium, phosphate, calcium, and uric acid across days 1 to 15.
INCIDENCE OF TLS

$\frac{42}{111} = 37.83\%, \text{ 95\% C.I.} = 28.81-46.85$
### Serum Electrolyte Changes

**Medians of Electrolyte Levels Across Days**

- **Potassium**:
  - Day 0: 4.0
  - Day 1: 5.1
  - Day 2: 5.4
  - Day 3: 5.2
  - Day 4: 5.1
  - Day 7: 4.8
  - Day 15: 4.0

- **Phosphate**:
  - Day 0: 1.1
  - Day 1: 2.2
  - Day 2: 2.3
  - Day 3: 2.3
  - Day 4: 2.2
  - Day 7: 2.0
  - Day 15: 1.3

- **Calcium**:
  - Day 0: 2.3
  - Day 1: 2.3
  - Day 2: 2.3
  - Day 3: 2.3
  - Day 4: 2.3
  - Day 7: 2.4
  - Day 15: 2.4

- **Uric Acid**:
  - Day 0: 0.3
  - Day 1: 0.3
  - Day 2: 0.3
  - Day 3: 0.3
  - Day 4: 0.3
  - Day 7: 0.3
  - Day 15: 0.3

**Day of Observation**:
- Day 0
- Day 1
- Day 2
- Day 3
- Day 4
- Day 7
- Day 15
## TLS IN HAEMATOLOGICAL AND NON-HAEMATOLOGICAL TUMOURS

<table>
<thead>
<tr>
<th></th>
<th>HAEMATOLOGICAL</th>
<th>NON HAEMATOLOGICAL</th>
<th>TOTAL</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POSITIVE</strong></td>
<td>40 (75.47%)</td>
<td>2 (3.45%)</td>
<td>42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>NEGATIVE</strong></td>
<td>13 (24.53%)</td>
<td>56 (96.55%)</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>53 (100%)</td>
<td>58 (100)</td>
<td>111</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

- Incidence of TLS found in this study was 37.8%.
- About 720 patients receive chemotherapy annually.
- This means that about 273 patients are at risk of TLS per year.
- Case fatality rate of 4.76% may translate to 13 deaths per year.
- Preventable and treatable condition
DISCUSSION CTD

• Association between potassium and phosphate quite remarkable. Need for further study.

• The absence of hyperuricemia is unusual.

• Use of allopurinol prophylaxis in all the patients at risk.

• Could the results have been different without allopurinol prophylaxis?

❖ Moderate hyperphosphatemia was insufficient to cause hypocalcemia.
CONCLUSIONS:

✓ Tumour lysis syndrome is common at KNH (38.7%). It mainly occurs in haematological malignancies.

✓ Most cases of tumour lysis syndrome occur on the first day of chemotherapy.

✓ Hyperkalemia and hyperphosphatemia are the main manifestations of TLS at KNH.
RECOMMENDATIONS:

1) All patients with haematological malignancies receiving chemotherapy should have their electrolytes monitored for at least two days after initiation of therapy.

2) Patients who cannot afford to pay for uric acid, calcium, phosphate and potassium can be monitored for hyperkalemia alone.

3) Allopurinol prophylaxis should be continued.

4) Continuous retrospective analysis of TLS data.
ACKNOWLEDGEMENTS

Prof. N.A. ABINYA
Dr. M. JOSHI
Dr. A. AMAYO
Dr. H. ABWAO

All the staff in the haematology/oncology clinics and wards at KNH
- KONGOI MISSING FOR LISTENING